

REMARKS/ARGUMENTS

Applicant thanks the Examiner for the interview conducted on July 16, 2004 in which the 35 U.S.C. §112 rejection to claim 37 and the Gaskell reference were discussed. As a result of that interview, Applicants have amended claims 31, 33, and 37 for further consideration. After entry of the foregoing amendments, claims 31-33, 35-40, 42, 44-46 and 48 (2 independent claims; 14 total claims) remain pending in the application. Reconsideration is respectfully requested.

The Examiner has stated that the oath or declaration is defective because the address of inventor Krone is crossed out but not initialed and no date of amendment has been disclosed. The Examiner has required a new oath or declaration in compliance with 37 C.F.R. 1.67(a) identifying this application by application number and filing date. In response to the Examiner's statement, Applicant has attached hereto a new declaration in compliance with 37 C.F.R. 1.67(a).

Claims 37-40, 42, 44-46 and 48 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. In response to the Examiner's rejection, Applicants have amended claims 33 and 39 to correct the antecedent basis problem pointed out by the Examiner. The Applicants have also amended claim 37 to correct the vagueness and indefiniteness pointed out by the Examiner.

Claims 31 and 37 stand rejected under 35 U.S.C. §102(b) as being anticipated by Gaskell et al. (hereinafter "Gaskell"). In particular, the Examiner states that Gaskell discloses a method for detecting at least one analyte in which an internal standard is added to the sample containing analyte. The Examiner further states that Gaskell discloses capturing and isolating the analyte and internal standard with an affinity reagent and that this extract containing the analyte and internal standard is analyzed by GC-MS. The Examiner further states that Gaskell discloses that a standard curve is used for the quantitation of the analyte and internal standard. Finally, the Examiner states that Gaskell discloses that the standard curve was established by analysis of derivatized standard mixtures. Applicants respectfully traverse this rejection.

Gaskell is specifically directed to establishing fractionation procedures that complement the specificity of gas chromatography-mass spectrometry (GC-MS) detection. Applicants' claimed methods do not require gas chromatography either before, or in combination with, mass

spectrometry in order to achieve detection. Applicants have amended independent claims 31 and 37 to further identify the step of quantifying the one or more analytes by stating that this quantification step comprises using only mass spectrometric analysis. In that Gaskell fails to disclose using only mass spectrometric analysis for quantification, Gaskell cannot anticipate Applicants' claimed invention.

Claims 31-33 and 37-39 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Papac (Protein Science) in view of Gaskell. In particular, the Examiner states that Papac discloses antibodies immobilized to agarose beads and incubating the beads with antigens for a time period to allow the immobilized antibody to bind to the antigen to form a complex. The Examiner further states that Papac discloses centrifuging the complex and removing supernatant and adding matrix to the antibody/antigen complex. The Examiner also states that Papac discloses determining the identity of the analyte using mass spectrometry and mass to charge ratio. The Examiner concedes that Papac differs from the instant invention in failing to teach that the specimen is combined with an internal reference species of known concentration prior to the capturing and isolation step wherein both the analyte and the IRS are captured and isolated. However, the Examiner states that Gaskell discloses the addition of an internal standard to a specimen containing analytes and determining the analyte by mass spectrometry. The Examiner further states that Gaskell discloses capturing and isolating the analyte and internal standard with an affinity reagent, using a standard curve for the quantitation of the analyte and internal standard, and establishing the standard curve by analysis of derivatized standard mixtures. The Examiner further contends that Gaskell discloses that the addition of the internal standard to the specimen provides higher precision to the analytic procedures and that the immunoadsorption technique provides a rapid and convenient procedure for an analyte before analysis. Therefore, the Examiner contends that it would have been obvious to one of ordinary skill in the art to incorporate an internal standard and affinity reagents as taught by Gaskell into the method of Papac because Gaskell teaches that the addition of the internal standard to the specimen provides higher precision to the analytical procedures and also teaches that the immunoadsorption technique provides a rapid and convenient procedure for an analyte before analysis. Applicants respectfully traverse this rejection.

Papac (Protein Science) studies the interaction of a known purified sample. The identity of the monoclonal antibody used in Papac is already known and is not determined using mass

spectrometry. Further, as previously stated, Gaskell is specifically directed to establishing fractionation procedures that complement the specificity of gas chromatography-mass spectrometry (GC-MS) detection. Gaskell discloses using an internal standard in combination with both gas chromatography and mass spectrometry. In contrast, Applicants' claimed invention performs quantification of analytes with an internal reference species using only mass spectrometry. Therefore, it would not have been obvious to one of ordinary skill in the art to use the internal reference standard disclosed in Gaskell in the method used by Papac because, according to Gaskell, the internal reference standard must be analyzed by gas chromatography and mass spectrometry.

Claims 35, 36, 40 and 42 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Papac (Protein Science) and Gaskell in view of Papac (Analytical Chemistry). Although the Examiner concedes that Papac (Protein Science) differs from the instant invention in failing to disclose adding a disassociation agent to the isolated post-combination affinity reagent prior to the step of adding the laser desorption/ionization agent, the Examiner contends that Papac (Analytical Chemistry) discloses that sample preparation can influence the spectra observed in that for immobilized affinity chromatography, a three times stronger signal is observed when the supernatant is used for analysis compared with mixing the MALDI matrix with the beads on the target and that immobilized affinity chromatography differs from conventional chromatography in that it exploits specific biological interactions such as those of an antibody and antigen which demonstrate high specificity associated affinity binding and that, either half of a biological interaction can be used in the stationary phase as an immobilized ligand. Accordingly, the Examiner contends that it would have been obvious to one of ordinary skill in the art to incorporate the use of a disassociation reagent as taught by Papac (Analytical Chemistry) into the modified method of Papac (Protein Science) because Papac (Analytical Chemistry) shows that the disassociation reagent allows for a three times stronger signal. Applicants respectfully traverse this rejection.

As previously discussed above, the combination of Papac (Protein Science) and Gaskell would not be obvious to one of ordinary skill in the art. Therefore, it would not be obvious to one of ordinary skill in the art to further combine Papac (Analytical Chemistry) with these two references to arrive at Applicants' claims 35, 36, 40 and 42.

Claims 44-46 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Papac (Protein Science) and Gaskell in view of Merren, U.S. Patent No. 3,770,337 (hereinafter “Merren”). Although the Examiner concedes that Papac (Protein Science) and Gaskell differ from the instant invention in failing to specifically teach interpolating the analyte species mass spectrometric response to the IRS’s mass spectrometric response, the Examiner contends that Merren teaches the addition of a reference substance which provides a spectrum containing peaks at several known mass-to-charge ratios. The Examiner further states that Merren teaches that the reference spectrum is accurately correlated with the spectrum of the unknown substance and that the reference peaks act as accurate markers forming a calibrated scale from which the mass-to-charge ratios of peaks of the unknown substance are interpolated. The Examiner finally states that Merren teaches that this provides a method for combining signals representative of the simultaneous spectral analysis of two substances, thereby permitting single channel processing of the combined signal. Accordingly, the Examiner contends that it would have been obvious to one of ordinary skill in the art to interpolate the analyte species and the reference species as taught by Merren into the modified method of Papac (Protein Science) because Merren shows that this provides a method for combining signals representative of the simultaneous spectral analysis of two substances, thereby permitting single channel processing of the combined signal. Applicants respectfully traverse this rejection.

As previously explained above, it would not be obvious to one of ordinary skill in the art to combine Papac (Protein Science) and Gaskell because Gaskell discloses the need to use both gas chromatography and mass spectrometry in analyzing the internal reference standard. Therefore, since it would not be obvious to one of ordinary skill in the art to combine Papac (Protein Science) and Gaskell, it would not be obvious to one of ordinary skill in the art to further combine Merren with these references.

Claim 48 stands rejected under 35 U.S.C. §103(a) as being unpatentable over Papac (Protein Science) and Gaskell in view of Papac (Analytical Chemistry) as applied to claims 31-33, 35-40, and 42 above, and further in view of Merren. Although the Examiner concedes that Papac (Protein Science), Gaskell and Papac (Analytical Chemistry) differ from the instant invention in failing to specifically teach interpolating the analyte species’ mass spectrometric response to the IRS’s mass spectrometric response, the Examiner contends that Merren teaches the addition of a reference substance which provides a spectrum containing peaks at several

known mass-to-charge ratios. The Examiner then repeats his statements regarding additional teachings of Merren and contends that it would have been obvious to one of ordinary skill in the art to interpolate the analyte species and the reference species as taught by Merren into the modified method of Papac (Protein Science) because Merren shows that this provides a method for combining signals representative of the simultaneous spectral analysis of two substances, thereby permitting single channel processing of the combined signal. Applicants respectfully traverse this rejection.

As previously stated above, it would not have been obvious to one of ordinary skill in the art to combine the Papac (Protein Science), Gaskell, and Papac (Analytical Chemistry) references. Therefore, it would not have been obvious to one of ordinary skill in the art to further combine these references with Merren to arrive at Applicants' claim 48.

In view of the foregoing, Applicants respectfully submit that all of the pending claims fully comply with 35 U.S.C. §112 and are allowable over the prior art of record. Reconsideration of the application and allowance of all pending claims is earnestly solicited. Should the Examiner wish to discuss any of the above in greater detail or deem that further amendments should be made to improve the form of the claims, then the Examiner is invited to telephone the undersigned at the Examiner's convenience. The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account No. 19-2814. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

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